

Summary of Research Activities by Key Approach and Resource

Epidemiological and Longitudinal Studies

In 2008, the world's most comprehensive and longest running longitudinal examination of human aging celebrated an astonishing 50 years of groundbreaking research that has transformed the field of geriatrics. Since its establishment in 1958, the NIH-supported [Baltimore Longitudinal Study of Aging \(BLSA\)](#) has provided a wealth of information on the physical consequences of aging and has helped distinguish changes due to aging from those due to disease. For example, BLSA scientists have elucidated the relationship between age-related changes in the arteries and cardiovascular disease and also have distinguished normal age-related declines in cognitive ability from those associated with Alzheimer's disease and related conditions. In 2009, BLSA launched a new initiative called IDEAL (Insight into the Determinants of Exceptional Aging and Longevity), which will study people 80 years of age and older who are living free of physical and cognitive disease. This effort will help identify the genetic, environmental, social, and behavioral factors that allow some individuals to enjoy excellent health well into their 80s while others experience disease and physical decline earlier in life.

Introduction

Epidemiological studies examine factors that contribute to health and disease in human populations using a broad range of approaches. Persons or groups can be followed over time in longitudinal studies, or a snapshot of information can be collected at a single point in time. Studies can be done retrospectively, examining outcomes that have already occurred and factors that may have contributed to health or disease, or they can be done prospectively by beginning to monitor a population of interest before a particular disease-related outcome occurs. Many epidemiological studies are observational in nature, collecting information about and comparing groups—called cohorts—made up of individuals who share a characteristic of interest (e.g., tobacco use, age, educational status). Population studies are another type of epidemiological research, aimed at providing a better understanding of populations—how they change in size, composition, and distribution; the complex social, economic, and cultural factors that cause such changes; and the consequences of population change for health and well-being at the individual and societal levels.

Epidemiological research is a critical part of the activities undertaken to fulfill the NIH mission of pursuing fundamental knowledge of living systems and applying that knowledge to extend healthy life and reduce the burdens of illness and disability. Epidemiological research is important for investigating all types of disease and draws on expertise from a wide range of disciplines; thus, it is not surprising that virtually all NIH ICs are involved with epidemiological research in some capacity. As part of the continuum from basic to applied research, epidemiological and longitudinal studies often test the findings of laboratory or clinical research at the population level. For example, animal studies demonstrating the reproductive and neurological effects of bisphenol A (BPA)—a common component of plastics—have prompted large-scale epidemiological studies to ascertain the exposure and health effects of this chemical in humans. Additionally, observations made through epidemiological studies often result in the formulation of new or modified hypotheses that spur new basic, translational, and clinical studies. For example, epidemiological studies in the 1950s showing that tobacco smoking increases risk of lung cancer led to extensive research to identify the carcinogens and mechanisms involved in tobacco-related carcinogenesis. Thus, epidemiological and longitudinal studies are essential for linking bench to bedside to population.

Animal studies demonstrating the reproductive and neurological effects of bisphenol A (BPA)—a common component of plastics—have prompted large-scale epidemiological studies to ascertain the exposure and health effects of this chemical in humans.

The population-based perspective provided by epidemiological studies often helps to form a foundation for the practical application of scientific knowledge, such as changes in clinical practice and the development of public policy. For example, the Framingham Heart Study, which was initiated in 1948, linked risk of cardiovascular disease, which was rapidly becoming a major public health concern by the middle of the 20th century, to factors such as high serum cholesterol levels, hypertension, and cigarette smoking. Based on these results, clinicians were better able to identify patients at high risk for cardiovascular disease. More recently, a series of NIH studies revealed an increased risk of cancer following exposure to benzene at levels below 10 parts per million and documented blood toxicity following exposure levels of under 1 part per million.^{1, 2} These data were used by the U.S. Environmental Protection Agency (EPA) as it developed a new rule in 2007 that limits the benzene content in gasoline and adopts new standards for passenger vehicles and portable fuel containers to limit emissions of benzene and other hazardous air pollutants.³

Many of the NIH-supported epidemiological studies described in this section will inform future clinical practice guidelines and public policy, although it sometimes takes decades for the fruits of these large-scale, long-term studies to be realized. As the Nation's leading Federal agency for biomedical research, NIH is well suited to conduct these sorts of studies. Its stable infrastructure allows it to invest in the types of decades-long projects that are particularly informative for studying factors that contribute to disease development. Furthermore, NIH fosters team science among and between intramural and extramural scientists with diverse expertise, facilitating multidisciplinary studies that lead to a comprehensive understanding of health and disease.

¹ Hayes RB, et al. *J Natl Cancer Inst* 1997;89(14):1065-71. PMID: 9230889.

² Lan Q, et al. *Science* 2004;306(5702):1774-6. PMID: 15576619. PMCID: PMC1256034.

³ U.S. Environmental Protection Agency. Control of hazardous air pollutants from mobile sources: final rule to reduce mobile source air toxics. EPA420-F-07-01. February 2007. Available at <http://www.epa.gov/oms/regs/toxics/420f07017.htm#program>. Accessed July 30, 2009.

Catalog of Epidemiological & Longitudinal Research Activities

Currently, NIH does not collect the information necessary for a catalog of epidemiological studies and longitudinal studies. This capacity is expected to be developed in the future for integration with RCDC.

Summary of NIH Activities

Although not comprehensive, the following summary highlights several ongoing NIH-supported epidemiological and longitudinal studies. These examples illustrate the strengths of NIH's epidemiological research portfolio: continuing efforts to make the most of past investments, an appreciation of the myriad factors that contribute to health and disease, and cooperation within and beyond the biomedical research community to achieve outcomes relevant to public health.

Investments in the Past Continue to Pay Off

NIH has been investing in epidemiological and longitudinal studies for most of its history. Some of these

studies have been ongoing for decades. For example, the [Framingham Heart Study](#) has been running for more than 60 years. The infrastructure created and data collected from these studies continue to advance understanding of disease and health in new and exciting ways. Prolonged follow up also has enormously increased the value of these studies, and their existence helps form the foundation for extraordinary opportunities in biomedical research today.

NIH has been investing in epidemiological and longitudinal studies for most of its history. Some of these studies have been ongoing for decades.

Continuing to Follow Existing Cohorts

It has become clear that many of the factors contributing to health and disease are present and begin to exert their influence long before clinical presentation of a problem. NIH-supported longitudinal studies of many cohorts conducted over the past several decades are continuing to elucidate how diverse factors integrate and interact to contribute to disease over time as well as answering new research questions. The [National Longitudinal Study of Adolescent Health \(Add Health\)](#) is one example. It was established as a joint effort of 18 NIH Institutes and other Federal offices to examine how families, peers, schools, and neighborhoods influence the health-related behaviors of teens and their use of health care. During the first wave of the study in 1994-1995, information was collected through administration of more than 90,000 surveys to students in grades 7 through 12 and 20,000 at-home interviews with students and their parents. Follow up was conducted with the adolescents 1 year later and again in 2001-2002. Another round of follow up with the original Add Health cohort, now 24 to 32 years of age, was initiated in 2008. The social, behavioral, environmental, and biological data collected through this wave of the study will provide insight into developmental and health trajectories as adolescents move into young adulthood and assume adult roles and responsibilities. For example, one recent analysis revealed that individuals who married or moved in with a partner were more likely to become obese than those who were dating, suggesting that interventions targeted at those establishing a shared household may be useful.⁴ More than 600 publications have been generated based on Add Health data, which continue to be available for both scientific study and policy analyses.

The social, behavioral, environmental, and biological data collected through the National Longitudinal Study of Adolescent Health (Add Health) study will provide insight into developmental and health trajectories as adolescents move into young adulthood and assume adult roles and responsibilities.

⁴ The NS, Gordon-Larsen P. *Obesity* 2009;17(7):1441-7. PMID: 19360012. PMCID: PMC2745942.

Using Specimens from Existing Cohorts to Identify Genetic Markers of Disease

In addition to following cohorts for extended periods of time, NIH is leveraging its past and current investments in population-based studies to study the genetic basis of disease. The [Cancer Genetic Markers of Susceptibility \(CGEMS\)](#) project has conducted genome-wide association studies (GWAS) to identify genetic variants associated with risk of prostate and breast cancer using specimens from 11 existing cohorts. CGEMS researchers have identified new genetic variants in two regions of DNA (located on chromosomes 1 and 14) that may be associated with risk of sporadic breast cancer, as well as regions of chromosomes 7, 8, 10, and 11 that are associated with moderate increases in the risk of prostate cancer.^{5,6,7} The same region on chromosome 8 also may be involved in colon cancer and

certain other tumors, suggesting a novel pathway of cancer susceptibility shared by a variety of cancers.

The Cancer Genetic Markers of Susceptibility project has identified genetic variants associated with breast and prostate cancer, as well as a chromosomal region of shared susceptibility for several other cancers.

Another NIH initiative called the [SHARE \(SNP Health Association Resource\)](#) project also is conducting GWAS on several large cohorts to elucidate genetic contributors to disease. One of the cohorts being examined as part of SHARE is that of the [Framingham Heart Study](#). The Framingham cohort was first established in 1948 and has since been expanded to include the children and grandchildren of the original participants. As part of SHARE, the DNA of more than 9,000 Framingham participants from all three generations has been analyzed. These genetic data, along with information about major disease risk factors (e.g., systolic blood pressure, cholesterol levels, cigarette use), have been added to [dbGaP \(the database of Genotypes and Phenotypes\)](#) and are available for use by researchers interested in investigating genetic contributors to disease.

⁵ Thomas G, et al. *Nat Genet* 2009;41(5):579-84. PMID: 19330030.

⁶ Thomas G, et al. *Nat Genet* 2008;40(3):310-5. PMID: 18264096.

⁷ Yeager M, et al. *Hum Genet* 2008;124(2):161-70. PMID: 18704501. PMCID: PMC2525844.

Gaining Insights for Policy from Long-Term Population-Based Studies

Long-term NIH studies also have been used to inform the decisions of policymakers and assess the short- and long-term effects of policies on health or health-related behaviors. In 1975, NIH launched [Monitoring the Future](#) (MTF), a study that tracks the beliefs, attitudes, and behaviors of adolescents and young adults. MTF surveys approximately 50,000 students in grades 8, 10, and 12 each year. In addition, follow up is conducted with a subset of each graduating class until they reach age 30. Among other things, MTF gathers information on alcohol and other drug use, allowing identification of emerging substance abuse trends as well as factors contributing to them. MTF data have informed policy discussions on substance abuse and have been used by the White House Office of National Drug Control Policy to monitor progress toward national health goals. The most recent MTF survey, conducted in 2008, found that the rate of cigarette smoking was the lowest it has been in the 33-year history of the survey. The survey also revealed a 25 percent decline since 2001 in student reports of illicit drug use in the past month. However, after exhibiting consistent declines since the mid-1990s, marijuana use appears to have leveled off. Moreover, prescription drugs are now among those most commonly abused by high school seniors, following marijuana, alcohol, and tobacco.⁸

In 2008, the Monitoring the Future study found that the rate of cigarette smoking among students in grades 8, 10, and 12 was the lowest it has been in the 33-year history of the survey.

The increasing age of the U.S. population has major implications for policy. The NIH [Health and Retirement Study \(HRS\)](#) collects multidisciplinary data about the physical and mental health, insurance coverage, financial situations, family support systems, work status, and retirement planning of

Americans over age 50 to help inform policy decisions. Now in its 16th year, HRS surveys more than 22,000 Americans every 2 years. Nearly 1,000 researchers have used HRS data to publish more than 1,000 reports, including more than 600 peer-reviewed journal articles and book chapters, and 70 doctoral dissertations.⁹ Recently, HRS data were used to measure health insurance coverage trends as people approach and pass the age of eligibility for Medicare. The analysis found differential results for particular populations. For example, people who were unmarried or individuals in particularly good or poor health had an increased likelihood of being uninsured prior to becoming eligible for Medicare. Individuals in good health may have believed they did not need insurance while those in poor health may not have been able to obtain coverage. Nonwhites and those in good health had an increased likelihood of having Medicare-only coverage after reaching the age of eligibility for Medicare.¹⁰

⁸ National Institute on Drug Abuse. Monitoring the Future National Results on Adolescent Drug use: Overview of Key Findings 2008. Available at: <http://www.monitoringthefuture.org/index.html>. Accessed July 29, 2009.

⁹ National Institute on Aging. Growing Older in America: The Health & Retirement Study. March 2007. Available at <http://hrsonline.isr.umich.edu/index.php?p=dbook>. Accessed July 29, 2009.

¹⁰ Caffrey C, Himes CL. *J Aging Soc Policy* 2008;20(1):29-44. PMID: 18198158.

Pursuit of a Comprehensive Understanding of Health and Disease

A comprehensive understanding of health and disease requires consideration of factors from the molecular to the community level. Integration of this information necessitates a systems approach that takes into account genetics, biology, and the social sciences. Conducting studies in diverse contexts helps to elucidate how these contributors converge to influence health and also ensures that insights gained will benefit different populations. NIH supports a number of studies in the United States and worldwide aimed at building a comprehensive understanding of disease and health with the goal of identifying new and more effective approaches for prevention and treatment.

Determining How Genes and Environment Interact to Influence Disease Risk

With the availability of high-throughput sequencing technology and the completion of the Human Genome Project, research on the genetic basis of disease has exploded over the past 2 decades. More recently, it has become clear that environmental factors can have a strong influence on how genetic background affects disease risk. To facilitate research on the interactions of genes and the environment, NIH has launched a large volunteer DNA-banking project called the [Environmental Polymorphism Registry \(EPR\)](#). The goal of the EPR is to collect DNA samples from 20,000 individuals to allow scientists to study how genes contribute to diseases such as diabetes, heart disease, cancer, asthma, and many others. The study participants are in the greater Research Triangle Park region of North Carolina, which has a diverse population in terms of age, ethnicity, economic and educational background, and health status. Unlike anonymous DNA registries, researchers using EPR are able to identify and contact registry participants—with their consent—for further study if they are found to have potentially significant genetic variants. Another unique feature of the EPR is that two distinct populations are solicited for participation: an apparently healthy population as well as a population recruited from various clinics and hospitals in the area. Individuals in the clinic population have an array of medical conditions; their inclusion in the EPR increases the likelihood of identifying subjects with both the genetic and clinical characteristics of interest. These aspects of the EPR give scientists the flexibility to design follow-up studies while reducing biases that can occur in genetic epidemiology studies when subjects are recruited based primarily on their observable clinical or physical traits. Although many genes will be studied as part of the EPR, the focus will be on so-called "environmental response genes" that increase or decrease disease risk when combined with an environmental exposure.

The Environmental Polymorphism Registry will collect DNA from 20,000 people to allow scientists to study how genes contribute to diseases such as diabetes, heart disease, cancer, asthma, and many others.

Through the [Breast Cancer and the Environment Research Centers \(BCERC\)](#), NIH is studying how interactions of chemical, physical, and social factors, combined with genetic factors, affect breast development during puberty and breast cancer predisposition. An epidemiologic study being conducted as part of BCERC is prospectively following through puberty a cohort of multiethnic 7- and 8-year-old girls from the Kaiser Foundation Health Plan. Other researchers are studying a population of white and African American public school students to see how diet influences fat tissue and alters the effects of hormones on sexual maturation. Endocrine disruptors, irradiation, and psychosocial elements also will be studied for effects. The BCERC directly relates to one of NIH's Government Performance and Results Act (GPRA) goals: By 2011, conduct studies of girls aged 6 through 8 years to determine the associations of 12 environmental exposures with age of onset of puberty and progression through puberty (SRO-5.10).

Improving Treatment and Prevention

In addition to providing a more complete picture of disease, multidisciplinary involvement is crucial for generating results with practical implications for clinical practice or behavior. Several ongoing NIH studies have the potential to alter clinical practice to improve health and minimize the burden of disease. The [Oral HIV/AIDS Research Alliance \(OHARA\)](#) is part of the AIDS Clinical Trials Group, the world's largest HIV clinical trials organization. OHARA drives and supports studies in the United States and internationally to improve diagnosis, treatment, and management of AIDS-related oral complications. These complications—which include ulcers and tumors, fungal infections, and painful viral lesions—occur in nearly all of the 33 million HIV-infected people worldwide and can compromise nutrition and exacerbate immune suppression. Although antiretroviral therapy alleviates some of the symptoms, many oral lesions require additional specific treatment. NIH provides central management and leadership for OHARA researchers, which include experts in epidemiology, mycology, and virology.

Through the [COPDGene](#) study, NIH is performing genetic testing in more than 10,000 current or former smokers to identify genetic characteristics associated with the presence of chronic obstructive pulmonary disease (COPD). This research should help reveal why some smokers develop serious lung disease while others do not. In addition to helping clinicians identify smokers at high risk for COPD, the study results likely will reveal molecular pathways involved in the pathogenesis of the disease that may be targets for prevention or therapy.

Identifying Disease Risk among Diverse Populations

Research has shown that factors such as genetic background, geographic location, socioeconomic status, and cultural traits can result in variations in disease risk among different populations. This observation has important implications for biomedical research, as results in one population may not necessarily apply to another. Thus, it is important to include study participants with diverse backgrounds and characteristics to increase the likelihood that insights gained through study findings will benefit all groups of people. In this regard, NIH is supporting the [Multi-Ethnic Study of Atherosclerosis \(MESA\)](#), a multicenter epidemiological study of cardiovascular disease in men and women from four ethnic groups—white, African American, Hispanic, and Chinese. This study, which began in 1999, has measured and compared the value of chest computed tomography (CT), cardiac magnetic resonance imaging, carotid ultrasound, arterial compliance, endothelial function, biochemical markers, and genetic and environmental factors for predicting the development of cardiovascular disease. In one recent study, researchers used MESA data to confirm that CT measurements of coronary calcium, previously shown to predict coronary heart disease among white populations, are effective predictors in African Americans, Hispanics, and Chinese as well.¹¹ Clinical and genomic data from the MESA cohort will be made

available to the research community through SHARe to facilitate GWAS.

The Multi-Ethnic Study of Atherosclerosis is studying cardiovascular disease in white, African American, Hispanic, and Chinese populations.

¹¹ Detrano R, et al. *N Engl J Med* 2008;358(13):1336-45. PMID: 18367736.

Culture of Cooperation to Promote Public Health

Bridging the gap between research and application requires the contributions of numerous scientists with diverse expertise. NIH therefore fosters a culture of cooperation, encouraging researchers to build teams capable of designing and conducting research with identified potential to improve public health.

Teaming Up to Improve the Study of Disease

Recognizing the need for large-scale collaborations to study the role of gene-gene and gene-environment interactions in the etiology of cancer, NIH formed the [Cohort Consortium](#). The mission of the Consortium—which currently comprises 37 cohorts and more than 4 million individuals—is to foster communication among investigators leading cohort studies of cancer; promote collaborative projects for topics not easily addressed in a single study; and identify common challenges in cohort research and search for solutions. Investigators team up to use common protocols and methods to facilitate parallel and pooled analyses of data. In addition to the CGEMS initiative (described above), another project of the Cohort Consortium is the Pancreatic Cancer Cohort Consortium in which investigators from 12 prospective epidemiologic cohort studies and 1 case-control study are collaborating to carry out whole-genome scans of common genetic variants to identify markers of susceptibility to pancreatic cancer.

Bringing Together NIH Institutes and Centers

The 27 NIH ICs collectively house expertise on a broad spectrum of diseases, populations, and research support methods. Large-scale epidemiological studies provide an ideal opportunity for researchers from the various NIH components to come together to conduct innovative studies on the diverse factors that coalesce to influence public health and disease. One example of collaboration among NIH ICs is the [Hispanic Community Health Study](#), which is sponsored by six NIH Institutes (NHLBI, NCMHD, NIDCD, NIDCR, NIDDK, and NINDS) and the NIH Office of Dietary Supplements. This multicenter study aims to recruit 16,000 persons of Hispanic/Latino descent, with a focus on individuals with Cuban, Puerto Rican, Mexican, and Central/South American ancestry. Participants will undergo a series of physical examinations and interviews to identify factors that influence a wide variety of diseases, disorders, and conditions, including heart disease, asthma, sleep disorders, diabetes, cognitive impairment, and more. Particular attention will be given to the role of cultural adaptation and disparities in the prevalence and development of disease. The insights gained from this study will be invaluable because the U.S. Hispanic population, already the largest minority population in the country, is expected to triple by 2050.

The Hispanic Community Health Study will provide insight into the prevalence of and risk factors for a variety of diseases within the most rapidly growing ethnic population in the United States.

Collaborating with Other Federal Departments and Agencies

As the Nation's premiere biomedical research agency, NIH seizes the opportunity to collaborate with other Federal departments and agencies on projects related to health. One example of such an intergovernmental collaboration is the [Agricultural Health Study \(AHS\)](#), cosponsored by two NIH Institutes and EPA. With a cohort of more than 89,000 private and commercial pesticide applicators and their spouses, the study is exploring occupational, lifestyle, and genetic factors that may affect the rate of diseases in farming populations. Although current medical research suggests that agricultural workers are healthier overall than the general U.S. population, they may have higher rates of some types of cancer and other conditions like asthma, neurologic disease, and reproductive problems. A recent AHS study found that elevated exposure to certain pesticides was associated with a doubling of the risk of adult-onset asthma.¹² Another study evaluated the relationship between lifetime exposure to pesticides and diabetes; of the 50 pesticides evaluated, 7 were associated with an increased risk of diabetes. The strongest association was with the organophosphate insecticide trichlorfon.¹³ Continuing identification of links between agricultural exposures and health problems will inform future policies designed to protect farmers, their families, and others who live or work in agricultural areas.

The Agricultural Health Study has linked exposure to certain pesticides to elevated risk of diabetes and adult-onset asthma.

NIH also is working with the U.S. Army to evaluate soldiers across all phases of Army service (e.g., predeployment training, deployment and noncombat assignments, and post-separation re-integration to civilian life) as part of the [Collaborative Study of Suicidality and Mental Health in the U.S. Army](#). This study was prompted by growing concern over the high rates of mental health and behavioral adjustment problems, including substance abuse and addiction, among recent U.S. military combat veterans and increasing rates of suicide among soldiers. The goal of the study is to identify modifiable risk and protective factors for, as well as moderators of, suicide-related behaviors. In a separate effort, three NIH Institutes, in conjunction with the Department of Veterans Affairs, have issued a [call](#) for studies examining how trauma, stress, and substance use/abuse emerge in U.S. military personnel, veterans, and their families, with a focus on how these disorders can be prevented and treated. NIH also is launching a study of the impact of existing national, state, and/or local community-based programs that are addressing the re-entry/adjustment and mental health needs of recent combat veterans. This initiative will inform strategic approaches to fostering the successful transition of all service members to civilian roles.

¹² Hoppin JA, et al. *Eur Respir J* 2009;34(6):1296-303. PMID: 19541724. PMCID: PMC2822385.

¹³ Montgomery MP, et al. *Am J Epidemiol* 2008;167(10):1235-46. PMID: 18343878. PMCID: PMC2832308.

Conclusion

Epidemiological and longitudinal studies are essential to NIH's efforts to bridge the results of basic, translational, and clinical studies to practical applications such as clinical practice and public policy. Many NIH epidemiological and longitudinal studies have had substantial influence on public health, with current investments likely to follow suit. This success is due to a number of factors, including investment in long-term studies, pursuit of a comprehensive view of disease, and promotion of a culture of cooperation.

The studies described above represent only a fraction of NIH's efforts in this area. Epidemiological studies are being carried out by experts in a number of disciplines, including, but not limited to, epidemiology, behavioral and social sciences, genetics, molecular biology, public health, economics, statistics, and data management. Although still far from comprehensive, additional notable examples of

NIH-supported epidemiological and longitudinal studies, as well as further information about some of the activities mentioned above, are found on the following pages.

Notable Examples of NIH Activity

Key

E = Supported through Extramural research

I = Supported through Intramural research

O = Other (e.g., policy, planning, or communication)

COE = Supported via congressionally mandated Center of Excellence program

GPRA Goal = Government Performance and Results Act

ARRA = American Recovery and Reinvestment Act

IC acronyms in **bold** face indicate lead IC(s).

Investments in the Past Continue to Pay Off

Population Research: Given the Nation's increasing diversity and changing demographics, it is critical to understand how trends in such areas as immigration, fertility, marriage patterns, and family formation affect the well-being of children and families. NIH research in these areas allows policymakers and program planners to better address public health needs. For instance:

- The Fragile Families and Child Well-Being Study follows children born to unmarried parents to assess how economic resources, father involvement, and parenting practices affect children's development.
- The New Immigrant Survey follows the first nationally representative sample of legal immigrants to the United States, providing accurate data on legal immigrants' employment, lifestyles, health, and schooling before and after entering the country.
- Several NIH Institutes are supporting The National Longitudinal Study of Adolescent Health, which integrates biomedical, behavioral, and social science data to discover the pathways that lead to health and/or disease in adulthood.
 - For more information, see <http://www.cpc.unc.edu/addhealth/>
 - For more information, see <http://nis.princeton.edu/index.html>
 - For more information, see <http://www.fragilefamilies.princeton.edu/index.asp>
 - This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*
 - (E) (**NICHD**, NCI, NCMHD, NIA, NIAAA, NIAID, NIDA, NIDCD, NINR, OAR, OBSSR, ORWH)

Genome-Wide Association Studies of Cancer Risk: The Cancer Genetic Markers of Susceptibility (CGEMS) project is a signature initiative that uses genome-wide association studies (GWAS) to identify genetic variants and mechanisms associated with cancer risk. Understanding these variants and mechanisms may lead to new preventive, diagnostic, and therapeutic interventions. CGEMS investigators have pinpointed genetic variants associated with elevated prostate cancer risk as well as variants associated with increased breast cancer risk. The same genetic variant was shown to be involved in increased prostate, colon, and other cancers, suggesting a common mechanistic pathway for susceptibility to a variety of cancers. Another GWAS project, the Cohort Consortium, is a unique extramural/intramural collaboration that allows Consortium partners to share access to data on 37 cohorts comprised of 4 million people from diverse populations. Each cohort contains extensive information on known or suspected risk factors and biospecimens collected pre- and post-diagnosis. The large number of study subjects permits the detection of modest genetic effects, as well as studies of

variants involved in less common cancers. One cohort within the Consortium, the Prostate, Lung, Colorectal, and Ovarian (PLCO) cohort, includes about 2.9 million specimens. These pre-diagnostic specimens provide a valuable resource for studies of cancer etiology and early detection. Researchers can correlate changes in molecular profiles associated with the onset of different types of disease, thereby providing valuable insights into the actual mechanisms of human carcinogenesis.

- For more information, see <http://cgems.cancer.gov>
- For more information, see <http://epi.grants.cancer.gov/Consortia/cohort.html>
- For more information, see <http://www.parplco.org>
- This example also appears in Chapter 2: *Cancer* and Chapter 3: *Genomics*
- (E/I) (NCI)

A Look at Drug Abuse Trends: Local to International: Two major systems of data collection are helping to identify substance abuse trends locally, nationally, and internationally: Monitoring the Future Survey (MTF) and the Community Epidemiology Work Group (CEWG). Both help to surface emerging drug abuse trends among adolescents and other populations, and guide responsive national and global prevention efforts. The MTF project, begun in 1975, has many purposes, the primary one being to track trends in substance use, attitudes, and beliefs among adolescents and young adults. The survey findings also have been used by the President's Office of National Drug Control Policy to monitor progress toward national health goals. The MTF project includes both cross-sectional and longitudinal formats—the former given annually to 8th, 10th, and 12th graders to see how answers change over time, and the latter given every 2 years (until age 30), then every 5 years to follow up on a randomly selected sample from each senior class. CEWG, established in 1976, provides both national and international information about drug abuse trends through a network of researchers from different geographic areas. Regular meetings feature presentations on selected topics, as well as those offering international perspectives on drug abuse patterns and trends. CEWG findings reported in 2008 and 2009 show decreases in methamphetamine indicators (e.g., treatment admissions), suggesting that the problems that had escalated in the first half of the decade may have stabilized or declined. Development of a Latin American Epidemiology Network is underway. NIH also has provided technical consultation for the planning and establishment of an Asian multicity epidemiological network on drug abuse.

- For more information, see <http://www.monitoringthefuture.org/>
- For more information, see <http://www.drugabuse.gov/about/organization/CEWG/CEWGHome.html>
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*
- (E) (NIDA)

Advances in Minority Mental Health Research: Results from NIH's Collaborative Psychiatric Epidemiology Surveys (CPES) have continued to shed light on the risk, prevalence, and outcomes associated with mental disorders in minority populations. Two CPES surveys, the National Latino and Asian American Study (NLAAS), and the National Survey of American Life (NSAL), are large, nationally representative epidemiologic surveys that focus, respectively, on the mental health epidemiology of Latinos and Asians, and African Americans. Examples of important research that has emerged from the CPES include an FY 2009 study from the NSAL that found that African American teens, especially girls, are at increased risk for suicide attempts, even if they have not been diagnosed with a mental disorder. The study's findings may be used to improve clinicians' screenings for suicidal behavior among adolescent African Americans. Additionally, an FY 2009 study using data from the NLAAS and the National Co-morbidity Survey Replication found that previous research showing native-born Latinos to

be at higher risk for mental disorders than nonnative-born Latinos may not be true across all Latino subgroups. NLAAS researchers found that this widely reported phenomenon (the "immigrant paradox") was true in some subgroups, but it did not hold in others (e.g., among Puerto Ricans). The results emphasize the heterogeneity of the Latino population and suggest the importance of addressing this population's subgroups in future research.

- Joe S, et al. *J Am Acad Child Adolesc Psychiatry* 2009;48(3):271-82. PMID: 19182692. PMCID: PMC2760075.
- Alegria M, et al. *Am J Psychiatry* 2008;165(3):359-69. PMID: 18245178. PMCID: PMC2712949.
- For more information, see <http://www.nimh.nih.gov/science-news/2009/black-teens-especially-girls-at-high-risk-for-suicide-attempts.shtml>
- This example also appears in Chapter 2: *Minority Health and Health Disparities*
- (E) (NIMH)

Demographic and Economic Studies of Aging: NIH supports a number of studies on the demographic and economic changes in our society. The Health and Retirement Study (HRS) is the leading source of combined data on health and financial circumstances of Americans over age 50 and a valuable resource to follow and predict trends and help inform policies for an aging America. Now in its 16th year, the HRS follows more than 20,000 people at 2-year intervals and provides researchers with an invaluable and growing body of multidisciplinary data on the physical and mental health of older Americans, insurance coverage, finances, family support systems, work status, and retirement planning. Recently, researchers used HRS data on memory and judgment of a large subset of HRS participants to determine trends in cognitive status of those age 70 and older. The researchers found that cognitive impairment dropped from 12.2 percent in 1993 to 8.7 percent in 2002. The study recently has been expanded to include additional key constructs in cognitive aging. NIH also has renewed its program of Centers on the Demography and Economics of Aging to foster research in the demography, economics, and epidemiology of aging and to promote the use of important datasets in the field. The achievements of this program in past years were recognized in September 2008 by the Heidelberg Award for Significant Contributions to the Field of Gerontology, a triennial international competition.

- For more information, see <http://hrsonline.isr.umich.edu>
- For more information, see <http://agingcenters.org>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIA)

Database of Genotype and Phenotype (dbGaP): Research on the connection between genetics and human health and disease has grown exponentially since completion of the Human Genome Project in 2003, generating high volumes of data. Building on its established research resources in genetics, genomics, and other scientific data, NIH established dbGaP to house the results of genome-wide association studies (GWAS), which examine genetic data of de-identified subjects with and without a disease or specific trait to identify potentially causative genes. By the end of 2009, dbGaP included results from more than 40 GWAS, including genetic analyses related to such diseases as Parkinson's disease, ALS, diabetes, alcoholism, lung cancer, and Alzheimer's disease. dbGaP is the central repository for many NIH-funded GWAS to provide for rapid and widespread distribution of such data to researchers and accelerate the understanding of how genes affect the susceptibility to and severity of disease.

- For more information, see <http://view.ncbi.nlm.nih.gov/dbgap>
- This example also appears in Chapter 3: *Genomics* and Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*

- (I) (NLM)

Epidemiologic Studies of Osteoporosis: NIH supports several prospective cohort studies, including the Study of Osteoporotic Fractures (SOF) in women and Mr. OS, a study of osteoporosis and other age-related diseases in men. The studies, which have been underway since 1986 and 1999, respectively, identified characteristics associated with fracture risk in older Americans. Assessing risk is important because the devastating consequences of low bone mass can be prevented. For example, simple changes to a person's home (e.g., adding more lights, removing clutter) can prevent falls. A balanced diet and modest exercise build bone strength, and medications can slow disease progression. SOF, Mr. OS, and other studies are providing information about osteoporosis diagnosis, treatment, and prevention. SOF and Mr. OS reinforced a notion, outlined in the Surgeon General's 2004 report on Bone Health and Osteoporosis, that older people who have a fracture should be tested for osteoporosis—even if the fracture occurred because of a traumatic injury (e.g., a fall off a ladder or an auto accident) that could hurt a healthy young person. Mr. OS is generating data that the U.S. Preventive Services Task Force can incorporate into guidance on using bone mineral density to assess fracture risk. Scientists using data from the Framingham Osteoporosis Study recently reported that men and women who consumed the most vitamin C had fewer hip fractures than those who consumed less vitamin C—a finding that may have implications for the recommended intakes established for vitamin C. Women's Health Initiative investigators demonstrated that low blood levels of vitamin D, which helps the body absorb calcium from food, also is associated with hip fracture risk.

- Cawthon PM, et al. *J Bone Miner Res* 2009;24(10):1728-35. PMID: 19419308. PMCID: PMC2743283.
- Cauley JA, et al. *Ann Intern Med* 2008;149(4):242-50. PMID: 18711154. PMCID: PMC2743412.
- Mackey DC, et al. *JAMA* 2007;298(20):2381-8. PMID: 18042915.
- Sahni S, et al. *Osteoporos Int* 2009;20(11):1853-61. PMID: 19347239. PMCID: PMC2766028.
- For more information, see http://www.niams.nih.gov/News_and_Events/Press_Releases/2007/11_28.asp
- For more information, see http://www.niams.nih.gov/News_and_Events/Spotlight_on_Research/2009/low_vitD_hip_fracture.asp
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIAMS, NCRR, NHLBI, NIA)

Pursuit of a Comprehensive Understanding of Health and Disease

Environmental Polymorphisms Registry: NIH, in collaboration with the University of North Carolina's General Clinical Research Center, has launched a large volunteer DNA banking project named the Environmental Polymorphisms Registry (EPR). The goal of the EPR is to collect DNA samples from 20,000 individuals in the greater Research Triangle Park region of North Carolina through local health care systems, study drives, health fairs, and other means. This area has a diverse population varying in age, ethnicity, economic and educational backgrounds, and health status. The EPR offers a valuable resource for human genomic studies, especially when compared to anonymous DNA registries. It was designed for scientists to screen for functionally significant alleles and to identify subpopulations of individuals with shared genotypes, and then correlate their genotypes with their phenotypes in a process known as "recruit-by-genotype." The value of the EPR lies in the ability to identify and then re-contact subjects with potentially significant polymorphisms for further study. A unique feature of the EPR is that two distinct populations are solicited, an apparently healthy population recruited from the general population as well as a clinic population recruited from various clinics and

hospitals in the area. Individuals in the clinic population have a wide array of medical conditions, and their inclusion in the EPR increases the likelihood of identifying subjects with both the genotypes and phenotypes of interest. These aspects of the EPR give scientists more flexibility in designing follow-up studies while reducing the ascertainment bias that can occur in genetic epidemiology studies when subjects are recruited based on phenotype.

- This example also appears in Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*
- (E/I) (NIEHS)

Understanding HIV, TB, and Malaria Co-infection: Tuberculosis (TB) is one of the leading causes of death among people living with HIV/AIDS and one of the most common opportunistic infections they experience. HIV and TB reinforce one another: HIV activates dormant TB in a person, who then becomes infectious and able to spread the TB bacillus to others. HIV infection increases the risk of getting TB by a factor of 20 or more, according to the World Health Organization. Similarly, many HIV-positive individuals are co-infected with malaria and face poorer treatment outcomes for both diseases. Notably, malaria infection in pregnant HIV-positive patients leads to worse outcomes for both the mother and the child. NIH is increasing its focus on TB co-infection with HIV, malaria, and other pathogens. Questions addressed include when to start antiretroviral therapy (ART) in patients co-infected with HIV and TB and how best to prevent development of active TB disease in HIV-infected individuals who are receiving ART. Other studies attempt to develop new diagnostics and TB treatments for individuals co-infected with TB and HIV. In addition, several studies underway assess how best to treat women and children with HIV and either TB or malaria. Finally, the Children with HIV and Malaria Project, a prospective, longitudinal study of Ugandan children, is designed to determine if HIV increases the risk of malaria in children, whether malaria is associated with accelerated HIV disease progression, if malaria treatment has a higher failure rate in HIV-infected children in comparison with HIV-uninfected children, and whether trimethoprim-sulfamethoxazole prophylaxis increases incidence of resistant malaria. The study enrolled 300 children with more than 3 years of follow-up, and concluded in September 2009.

- For more information, see http://www3.niaid.nih.gov/topics/HIVAIDS/Research/therapeutics/intro/drug_discovery.htm
- For more information, see <http://www3.niaid.nih.gov/topics/tuberculosis/>
- For more information, see <http://www.who.int/entity/tb/challenges/hiv/tbhivbrochure.pdf>
- For more information, see <http://www.unaids.org/en/policyandpractice/hivtreatment/coinfection/tb/default.asp>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*
- (E) (NIAID)

The Sister Study: Environmental Risk Factors for Breast Cancer: The NIH Sister Study prospectively examines environmental and familial risk factors for breast cancer and other diseases in a cohort of 50,000 sisters of women who have had breast cancer. The frequency of relevant genes and shared risk factors is greater among sisters, increasing the ability of the study to detect risks. Researchers will collect data on potential risk factors and current health status, and will collect and bank blood, urine, and environmental samples for future use in studies of women who develop breast cancer or other diseases compared with those who do not. Analysis of new cases will assess the separate and combined effects of environmental exposures and genetic variations that affect estrogen metabolism, DNA repair, and response to specific environmental exposures. Future analyses will focus on known and potential risk factors like smoking, occupational exposures, alcohol, diet and obesity, and include

analysis of phthalates, phytoestrogens, metals, insulin, growth factors, vitamins and nutrients, and genes in blood and urine. The study also allows investigators to examine a wide range of health outcomes of relevance to women, and to create a framework from which to test new hypotheses as they emerge. In addition to its focus on genetic and environmental causes of breast cancer, the prospective Sister Study tracks changes in health status over time. Among the chronic diseases currently studied are uterine fibroids and endometriosis, rheumatoid arthritis and other autoimmune diseases, thyroid disease, asthma, and cardiovascular diseases. As the cohort ages, the Sister Study will address aging-related health outcomes including osteoporosis, Parkinson's disease, and age-related cognitive decline.

- For more information, see <http://www.niehs.nih.gov/research/atniehs/labs/epi/studies/sister/index.cfm>
- This example also appears in Chapter 2: *Cancer*, Chapter 2: *Chronic Diseases and Organ Systems*, Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 2: *Minority Health and Health Disparities*
- (E/I) (NIEHS, NCMHD)

Breast Cancer and the Environment Research Centers: Researchers at the Breast Cancer and Environment Research Centers (BCERC) are investigating mammary gland development in animals, as well as in young girls, to determine vulnerability to environmental agents that may influence breast cancer development in adulthood. These efforts hopefully will lead to strategies that better prevent breast cancer. The purpose of the centers' program is to answer questions on how chemical, physical, biological, and social factors in the environment work together with genetic factors to cause breast cancer. Functioning as a consortium at four grantee institutions, the centers bring together basic scientists, epidemiologists, research translational units, community outreach experts, and community advocates. At one center, a sophisticated genomics and proteomics approach explores the impact of estrogenically active chemicals such as TCDD, bisphenol A, and phthalates, during early, critical periods of development. This is facilitated by advanced informatics at another major research institution. At another center, novel approaches to studying the impact of environmental exposures on interactions between epithelial cells and stromal cells are being studied. Normal and cancer-prone mice are being examined during various stages of development to determine the effects of exposure to multiple stressors as researchers are developing more sensitive screens for carcinogenicity. In concert with these studies, an epidemiological multi-ethnic study is examining and following through puberty a cohort of 7- and 8-year-old girls from the Kaiser Foundation Health Plan. Other researchers are studying a population of white and African American public school students to see how diet affects adipose tissue and alters hormonal control of sexual maturation. Endocrine disruptors, irradiation, and psychosocial elements also will be studied for effects.

- Lu P, Werb Z. *Science* 2008;322(5907):1506-9. PMID: 19056977. PMCID: PMC2645229.
Kouros-Mehr H, et al. *Cancer Cell* 2008;13(2):141-52. PMID: 18242514. PMCID: PMC2262951.
Welm BE, et al. *Cell Stem Cell* 2008;2(1):90-102. PMID: 18371425. PMCID: PMC2276651.
Kouros-Mehr H, et al. *Curr Opin Cell Biol* 2008;20(2):164-70. PMID: 18358709. PMCID: PMC2397451.
Ewald AJ, et al. *Dev Cell* 2008;14(4):570-81. PMID: 18410732. PMCID: PMC2773823.
Sternlicht MD, Sunnarborg SW. *J Mammary Gland Biol Neoplasia* 2008;13(2):181-94. PMID: 18470483. PMCID: PMC2723838.
Egeblad M, et al. *Dis Model Mech* 2008;1(2-3):155-67; discussion 165. PMID: 19048079. PMCID: PMC2562195.
Aupperlee MD, et al. *Endocrinology* 2009;150(3):1485-94. PMID: 18988671. PMCID: PMC2654739.
Lu P, et al. *Dev Biol* 2008;321(1):77-87. PMID: 18585375. PMCID: PMC2582391.
Jenkins S, et al. *Environ Health Perspect* 2009;117(6):910-5. PMID: 19590682. PMCID: PMC2702405.

- Teitelbaum SL, et al. *Environ Res* 2008;106(2):257-69. PMID: 17976571.
- Moral R, et al. *J Endocrinol* 2008;196(1):101-12. PMID: 18180321.
- Santos SJ, et al. *J Steroid Biochem Mol Biol* 2009;115(3-5):161-72. PMID: 19383543. PMCID: PMC2729057.
- Yang C, et al. *Reprod Toxicol* 2009;27(3-4):299-306. PMID: 19013232.
- Smith SW, et al. *J Health Commun* 2009;14(3):293-307. PMID: 19440911. PMCID: PMC2718320.
- J Health Psychol* 2008;13(8):1180-9. PMID: 18987091.
- Atkin CK, et al. *J Health Commun* 2008;13(1):3-19. PMID: 18307133.
- Kariagina A, et al. *Crit Rev Eukaryot Gene Expr* 2008;18(1):11-33. PMID: 18197783.
- Medvedovic M, et al. *Physiol Genomics* 2009;38(1):80-8. PMID: 19351911. PMCID: PMC2696152.
- Biro FM, et al. *J Pediatr Adolesc Gynecol* 2009;22(1):3-6. PMID: 19232295. PMCID: PMC2744147.
- For more information, see <http://www.bccrc.org/>
 - This example also appears in Chapter 2: *Cancer*, Chapter 2: *Life Stages, Human Development, and Rehabilitation*, Chapter 3: *Genomics*, Chapter 3: *Molecular Biology and Basic Research* and Chapter 3: *Clinical and Translational Research*
 - (E) (NIEHS, NCI) (GPRA)

Cancer Epidemiology Biomarkers and Prevention: The long-term Sister Study looks at the environmental and genetic characteristics of women whose sisters have had breast cancer to identify factors associated with developing breast cancer. A pilot study that was part of the Sister Study shows that women who maintain a healthy weight and who have lower perceived stress may be less likely to have chromosome changes associated with aging than obese and stressed women. Recently, NIH funded a study looking at 94 women whose breast cancer had spread or returned. Researchers asked the women whether they had ever experienced stressful or traumatic life events. The categories ranged from traumatic stress to some stress to no significant stress. The comparison revealed a significantly longer disease-free interval among women reporting no traumatic or stressful life events.

- For more information, see <http://www.niehs.nih.gov/news/releases/2009/sister-study.cfm>
- For more information, see <http://www.nlm.nih.gov/medlineplus/magazine/issues/winter08/articles/winter08pg6b.html>
- This example also appears in Chapter 2: *Cancer*
- (E/I) (NCI, NIA)

OHARA: The Oral HIV/AIDS Research Alliance: At the vanguard of basic, translational, and clinical research to combat the oral manifestations of HIV/AIDS is the NIH-funded Oral HIV/AIDS Research Alliance (OHARA), which drives and supports novel clinical studies in the United States and internationally to improve diagnosis, treatment, and management of comorbidities of AIDS-related oral complications, including necrotizing ulcers and tumors, fulminating fungal infections, and painful viral lesions that occur in almost all 33 million people infected worldwide. Their devastating effects compromise nutrition and exacerbate immune suppression in addition to the local effects. Even since the advent of antiretroviral therapy (ART), oral complications of AIDS remain a major public health problem. Though ART alleviates some symptoms, many oral lesions need additional specific treatment and globally, only 30 percent of HIV-infected individuals for whom ART is indicated receive it. The estimated prevalence of U.S cases of HIV/AIDS in 2006 exceeded 1.1 million, while about 56,300 people were newly infected with HIV that year. In its fourth year OHARA is making significant strides for people living with HIV/AIDS. OHARA is formed by world-expert scientists and clinicians. Its success is driven by three geographically and academically separate core units that provide expertise in epidemiology, mycology, and virology, embraced by a centralized NIH management and leadership. Currently, OHARA has ramped up eight clinical studies in various phases. They include studies to assess the clinical

effectiveness of diagnostic tools for HIV/AIDS-related conditions, and compare the safety and efficacy of novel treatments and preventive strategies for HIV/AIDS-related oral diseases and malignancies.

- Shiboski CH, et al. *J Oral Pathol Med* 2009;38(6):481-8. PMID: 19594839.
- Jacobson MA, et al. *PLoS One* 2009;4(4):e5277. PMID: 19381272. PMCID: PMC2667217.
- For more information, see <http://aactg.org/committees/scientific/optimization-co-infection-and-co-morbidity-management/subcommittees/ohara-sub-3>
- For more information, see <http://www.nidcr.nih.gov/Research/DER/IntegrativeBiologyAndInfectiousDiseases/AIDSImmuno.htm>
- For more information, see <http://aactg.org/about-aactg>
- For more information, see <http://www.who.int/hiv/data/en/>
- For more information, see <http://www.cdc.gov/hiv/topics/surveillance/basic.htm#Main>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense* and Chapter 3: *Clinical and Translational Research*
- (E) (NIDCR, NIAID)

The Role of Development in Drug Abuse Vulnerability: NIH supports animal, clinical, and epidemiological research across the lifespan to examine how developmental stage may influence drug abuse vulnerability or protection. The discovery of a protracted period of brain changes during early development and beyond has been critical to understanding the role of brain maturation in decision-making processes and responses to stimuli, including early (e.g., in utero) exposure to drugs. Adolescence has emerged as a particularly vulnerable period, during which an immature brain circuitry can translate into a preponderance of emotional reactivity (vs. higher cognitive control) that gives rise to the impulsive characteristics of many teenagers. This in turn may lead to dangerous risk-taking, such as experimenting with drugs that ultimately can lead to addiction. Using both animal models and clinical research, scientists are beginning to understand how environmental variables can play a key role in shaping brain maturation trajectories. In this regard, imaging, genetic, and epigenetic tools are helping interpret the effects of myriad environmental influences, such as quality of parenting, drug exposure, socioeconomic status, and neighborhood characteristics on brain development and behavior. In addition, the field of social neuroscience is harnessing the power of multidisciplinary approaches to tease apart these multilevel phenomena to better understand, for example, the neural mechanisms of peer pressure, the connections between chronic stress and risk of drug abuse initiation, and the impact that different early rearing environments can have on gene expression and behavior.

- For more information, see <http://www.nida.nih.gov/tib/prenatal.html>
- For more information, see <http://www.nida.nih.gov/scienceofaddiction/>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System*, Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 3: *Molecular Biology and Basic Research*
- (E) (NIDA, NICHD) (GPRA)

Following up on the Multimodal Treatment Study of Children with ADHD (MTA): Children with attention deficit hyperactivity disorder (ADHD), the most common of the psychiatric disorders that appear in childhood, often raise great concern from their parents and teachers because of their inability to focus on or finish tasks. Over time, these children may develop other emotional problems, including mood disorders, loss of self-esteem, and substance abuse. To address these issues, NIH is sponsoring an ongoing, multisite, follow-up of children from the MTA study—a treatment trial of nearly 600 ADHD-diagnosed elementary school children. Findings from the original MTA showed that long-term combination treatment (medication and psychosocial/behavioral treatment), as well as medication-management alone, significantly were superior to intensive behavioral treatments and routine community

care in reducing ADHD symptoms. In the follow-up study (n = 485 10 to 13 year olds), children from this cohort and others who received similar pharmacotherapy were assessed for substance abuse outcomes. The study found that despite treatment, children with ADHD showed significantly higher rates of delinquency and substance abuse. Follow-up of the MTA sample is continuing as the participating children go through adolescence and enter adulthood.

- Molina BS, et al. *J Am Acad Child Adolesc Psychiatry* 2009;48(5):484-500. PMID: 19318991.
- For more information, see <http://www.drugabuse.gov/CTN/protocol/0028.html>
- For more information, see <http://www.drugabuse.gov/CTN/protocol/0029.html>
- For more information, see <http://www.nida.nih.gov/ResearchReports/comorbidity/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIDA, NIMH)

The Early Childhood Longitudinal Study (ECLS) program: The National Center for Education Statistics, within the Institute of Education Sciences of the U.S. Department of Education, is conducting an ongoing study of a nationally representative sample of children from diverse socioeconomic and racial/ethnic backgrounds who will start kindergarten in 2011. Several Federal agencies, including NIH, are partnering on the study to determine how a variety of home, school, community, and student factors influence the transition of children to school; frame their early school experiences; shape their later school experiences; relate to normal cognitive, social, emotional, and physical child development; and affect academic performance over time. NIH is participating in a field test to work out logistics to determine the feasibility of adding a hearing and vision screening examination in the ECLS. ECLS is the only recent, nationally representative data collection program that enables statistical analysis of relationships between hearing and communication impairments or disorders and subsequent child development from infancy through eighth grade. The intent is to measure the hearing and vision of children during their first year of formal schooling, find out how hearing and vision change as a child grows, establish whether hearing and vision influence other aspects of normal child development, and clarify whether academic performance is influenced by hearing and vision. This information can be used then to evaluate how well early identification and intervention strategies were implemented during the birth cohort years from an earlier ECLS study.

- For more information, see <http://nces.ed.gov/ECLS/>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NEI, NIDCD)

HIV/AIDS Epidemiological and Long-Term Cohort Studies: NIH continues its support of the largest HIV/AIDS observational studies in the United States, the Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS) of homosexual and bisexual men. These studies repeatedly have made major contributions to our understanding of HIV transmission, disease progression, and best treatment practices. The WIHS, now in its 16th year of research, studies the natural history of HIV infection and AIDS progression in 2,404 HIV-infected and uninfected women, and bridges the gap between theoretic benefits and sustainable gains of antiretroviral therapy. The MACS, now in its 26th year of research, studies the natural history of HIV infection and AIDS progression in 6,973 homosexual and bisexual men at sites located in Baltimore, Chicago, Pittsburgh, and Los Angeles. These domestic cohorts are on the forefront of research to define the clinical manifestations of long-term HIV/AIDS infection. Data from these cohorts have resulted in published studies on the long-term risk of HIV/AIDS on cardiovascular disease. Studies have been initiated on aging, sleep disorders,

frailty, renal function, cognitive function, and behavior among HIV-infected persons.

- For more information, see <http://www3.niaid.nih.gov/about/organization/daids/daidsepi.htm>
- This example also appears in Chapter 2: *Infectious Diseases and Biodefense*
- (E) (NIAID, NCI, NCRR, NICHD, NIDA)

Multicenter AIDS Study (MACS) Small Grant Opportunity: MACS is an ongoing (since 1984) epidemiological study in several U.S. cities of multi-ethnic/racial HIV-infected and HIV-uninfected men who have sex with men (MSM). A small grant funding opportunity is enhancing the value and potential for new knowledge from the MACS by examining drug use and HIV/AIDS among MSM over the life course. Studies will include an examination of social and behavioral risk factors and trajectories, the role of drug use in neurocognitive function, and other medical consequences. Findings from these studies may lead to new insights and interventions targeting this high-risk group. Such findings reinforce the importance of implementing interventions targeting drug reduction as part of comprehensive and efficacious HIV prevention program.

- This example also appears in Chapter 2: *Infectious Diseases and Biodefense* and Chapter 3: *Clinical and Translational Research*
- (E) (NIAID, NIDA, NIMH)

National Epidemiologic Survey on Alcohol and Related Conditions: Predicting the First Use of Alcohol and Illicit Drugs and Correlated Brain Disorders: The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) collected comprehensive, detailed data from approximately 40,000 individuals on alcohol consumption, use of 10 categories of drugs, and symptoms of alcohol and specific drug use disorders, as well as mood, anxiety, and personality disorders in 2 separate waves. Results from the second wave of this nationally representative survey will provide predictors for the first incidence of substance abuse as well as mood and anxiety disorders. The rates of occurrence at 1 year of the survey were highest for alcohol abuse, alcohol dependence, major depressive disorder, and generalized anxiety disorder. The effects were much greater among men for substance use disorders and greater among women for mood and anxiety disorders, except for bipolar disorders and social phobia. African Americans were at decreased risk for alcohol abuse and Hispanic individuals were at decreased risk of generalized anxiety disorder. Substance abuse, mood disorders, and anxiety disorders occurred at similar or higher rates when compared to lung cancer, stroke, and cardiovascular disease. The higher incidence of all disorders in the youngest individuals highlights the need for increased vigilance in identifying and treating these disorders among young adults.

- Grant BF, et al. *Mol Psychiatry* 2009;14(11):1051-66. PMID: 18427559. PMCID: PMC2766434.
- (I) (NIAAA)

Building a Longitudinal Mental Health Tracking System: NIH has laid the initial groundwork to develop a mental health tracking system that will provide epidemiologic information on mental disorders on a continuing basis. By working with Federal agencies that currently conduct large-scale, ongoing national surveys, and adding detailed measures of mental health status, functioning, and service use, NIH will leverage existing resources to collect important mental health information in a cost-efficient manner. The longitudinal nature of the resulting data will provide NIH the ability to track the prevalence, incidence, severity, correlates, and trajectories of mental disorders, as well as related service use and outcomes, over time. The resulting data also could provide important information on key subgroups (e.g., racial/ethnic populations, people with autism) and geographic areas of varying sizes (e.g., states,

counties). These data are critical for targeting future research activities and ensuring the effectiveness of delivered interventions.

- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIMH)

The National Children's Study (NCS): NCS promises to be one of the richest information resources available for answering questions related to children's health and development and will form the basis of child health guidance, interventions, and policy for generations to come. The landmark study will examine the effects of environmental influences on the health and development of more than 100,000 children across the United States, following them from before birth until age 21. This extensive research effort will examine factors ranging from those in the natural and man-made environment to basic biological, genetic, social, and cultural influences. By studying children through their different phases of growth and development, researchers will be able to understand better the role of these factors in both health and disease. Specifically, the NCS will identify factors underlying conditions ranging from prematurity to developmental disabilities, asthma, autism, obesity and more. The study is led by a consortium of Federal agencies including NIH, CDC, and the EPA.

- For more information, see <http://www.nationalchildrensstudy.gov>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (I) (NICHD, NIEHS)

Fetal Alcohol Effects: The developing embryo and fetus is very vulnerable to the adverse effects of alcohol. Since Fetal Alcohol Syndrome was first recognized around 1970, NIH has supported research on outreach to pregnant women for identification and intervention of risky drinking; research to enhance our ability for early identification of and interventions with prenatal alcohol-affected children; research exploring nutritional and pharmacological agents that could lessen alcohol's adverse effects on the developing embryo/fetus; and research on how alcohol disrupts normal embryonic and fetal development. For example, a recent study with rats showed that choline, an essential nutrient, was found to effectively reduce the severity of some fetal alcohol effects, even when administered after the ethanol insult was complete. NIH also is investing in a large-scale prospective study looking at prenatal alcohol exposure along with other maternal risk factors in adverse pregnancy outcomes. Following a 3-year feasibility study, NIH established the Prenatal Alcohol, Sudden Infant Death Syndrome, and Stillbirth (PASS) Research Network, a multidisciplinary consortium to determine the role of prenatal alcohol exposure and other maternal risk factors in the incidence and etiology of sudden infant death syndrome (SIDS), stillbirth, and fetal alcohol syndrome, all of which are devastating pregnancy outcomes. The PASS study prospectively will follow 12,000 pregnant, high-risk, American Indian and South African women and their infants until the infants are 12 months old. Maternal, fetal, and infant measures and tissues will be obtained for analysis.

- For more information, see <http://www.nichd.nih.gov/research/supported/pass.cfm>
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation* and Chapter 2: *Minority Health and Health Disparities*
- (E) (NIAAA, NICHD)

Strategies to Manage and Prevent Food Allergies: Food allergy occurs in approximately 4.7 percent of children under 5 years of age and in 3.7 percent of children 5 to 17 years of age. Allergies to peanuts and tree nuts, the allergens most relevant to severe food allergy and anaphylaxis, occur in

approximately 1 percent of children and adults. Severe whole-body allergic reactions, also known as anaphylaxis, are a frequent cause of emergency room visits, many of which are attributed to food allergy. Every year in the United States, it is estimated that there are approximately 15,000-30,000 episodes of food-induced anaphylaxis. NIH seeks to understand better both the immune system response to food allergies and how certain foods trigger an allergic reaction. Researchers in the United States and abroad are conducting clinical trials to improve management of allergy to cow's milk, egg, and peanut, and innovative clinical trials are assessing strategies to prevent development of peanut allergies. One important trial will determine whether early and regular consumption of a peanut snack by infants and very young children at risk of developing peanut allergy will promote tolerance and prevent the development of this allergy. In FY 2008, NIH sought to bring new investigators into the field through the Exploratory Investigations in Food Allergy initiative, which supports innovative pilot studies and developmental research on the mechanisms of food allergy. The program will be recomputed in FY 2010. During this period, NIH continued funding for the Consortium of Food Allergy Research, which supports basic, preclinical, and clinical research to assess the pathophysiology and natural history of food allergy-associated anaphylaxis and to develop interventions to prevent and treat food allergy.

- For more information, see <http://www3.niaid.nih.gov/topics/foodAllergy/default.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Clinical and Translational Research*
- (E/I) (NIAID)

Eye Disease Burden Data from National Health and Nutrition Examination Survey

(NHANES): The CDC uses rigorous national surveys such as NHANES to collect information on the health of the U.S. population. In 1999, NIH and CDC collaborated to add estimates of vision impairment to NHANES. Based on an analysis of baseline NHANES data from 1999-2004, it was estimated that half of the U.S. population over the age 20 years has blurry vision, called refractive errors (nearsightedness, farsightedness, and/or astigmatism). Refractive errors can be corrected with eyeglasses, contact lenses, or surgery to restore clear vision. After 2004, a new survey was developed to capture information on more severe visual impairments, the extent of uncorrected (but correctable) refractive errors, the methods individuals selected to correct refractive error, and vision-related quality-of-life questions. These changes will improve estimates of the extent and nature of vision impairment in the United States. The effort to develop visual impairment statistics is consistent with an NIH GPRA goal to "develop stable national estimates of vision impairment by extending the vision component of NHANES."

- Vitale S, et al. *Arch Ophthalmol* 2008;126(8):1111-9. PMID: 18695106. PMCID: PMC2772054.
- For more information, see <http://archophth.ama-assn.org/cgi/content/full/126/8/1111>
- For more information, see <http://www.cdc.gov/nchs/nhanes.htm>
- (I, O) (NEI) (GPRA)

End-Stage Renal Disease: According to the United States Renal Data System—an NIH-supported national data system that collects, analyzes, and distributes information about people with kidney failure—more than one-half million Americans suffer from kidney failure. Patients with this condition—known as end-stage renal disease or ESRD—require a kidney transplant or hemodialysis, a process that uses a machine to remove waste products and excess fluid from the bloodstream. To facilitate hemodialysis, some patients undergo a surgical procedure to create a site on the body that allows easy, repeated access to the blood vessels. However, over time, many vascular access sites become unusable and fail. The NIH-supported Dialysis Access Consortium found that treatment with an anti-blood clotting drug did not improve the long-term suitability of a type of access known as a fistula. A

separate study by the consortium found that the long-term usability of a different type of access site, known as a graft, could be improved through treatment with a combination of aspirin and another anti-clotting drug. Still, important questions remain. To better understand the underlying biology of access site maturation, NIH is launching a Vascular Biology of Hemodialysis Vascular Access Consortium to study the molecular and cellular pathways that contribute to vascular injury and high rates of vascular access failure. Such research may inform new strategies to improve outcomes in patients undergoing hemodialysis.

- Dember LM, et al. *JAMA* 2008;299(18):2164-71. PMID: 18477783.
- Dixon BS, et al. *New Engl J Med* 2009;360(21):2191-201. PMID: 19458364.
- For more information, see <http://www.usrds.org>
- For more information, see <http://www.nih.gov/news/health/may2008/niddk-22a.htm>
- For more information, see <http://www.nih.gov/news/health/may2009/niddk-20.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*
- (E) (NIDDK)

Research on Bariatric Surgery: The multicenter NIH-funded Longitudinal Assessment of Bariatric Surgery (LABS) consortium is analyzing the risks and benefits of bariatric surgery as a treatment for extreme obesity in adults. Results from this study have been published in the *New England Journal of Medicine*. The study also addresses comparative effectiveness with respect to its collection of data on surgical procedures and pre- and post-operative information. Because bariatric surgery also is used in clinical practice sometimes as a treatment for severely obese adolescents, NIH additionally is supporting an observational study of teens already scheduled for surgery, Teen-LABS, to collect data to help determine whether it is an appropriate treatment option for extremely obese adolescents. A pilot study also is being conducted using the new Metabolic Clinical Research Unit at the NIH CC to examine changes in insulin resistance after bariatric surgery. To further explore the observation that certain bariatric surgical procedures are associated with amelioration of obesity-related insulin resistance and diabetes soon after surgery, and thus independent of weight loss, NIH issued a funding opportunity announcement to encourage research in this area.

- Adams TD, et al. *N Engl J Med* 2007;357(8):753-61. PMID: 17715409.
- The Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. *N Engl J Med* 2009;316(5):445-54. PMID: 19641201.
- For more information, see <http://win.niddk.nih.gov/publications/labs.htm>
- For more information, see <http://www.nih.gov/news/pr/apr2007/niddk-16.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Clinical and Translational Research*
- (E/I) (NIDDK, ORWH)

The Hispanic Community Health Study: In October 2006, NIH began the largest long-term epidemiological study of health and disease ever conducted in people of Hispanic/Latino heritage living in the United States. The study includes 16,000 participants of diverse Hispanic/Latino background, including Mexican, Cuban, Puerto Rican, and Central/South American. It is designed to identify factors that render these groups either susceptible to or protected from heart disease, stroke, asthma, chronic obstructive pulmonary disease, sleep disorders, dental disease, hearing loss, diabetes, kidney and liver disease, cognitive impairment, and other chronic conditions. Recruitment started in March 2008 in four cities. Variables such as height, weight, and other body measurements; blood pressure; blood lipids and glucose levels; diet; physical activity; smoking; acculturation; socioeconomic status; psychosocial factors; occupational history and exposure; access to and use of health care services; and use of

medications and dietary supplements currently are being assessed.

- For more information, see <http://www.csc.unc.edu/hchs>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Minority Health and Health Disparities*
- (E) (NHLBI, NCMHD, NIDCD, NIDCR, NIDDK, NINDS, ODP/ODS)

The Multi-Ethnic Study of Atherosclerosis: The Multi-Ethnic Study of Atherosclerosis (MESA) is a multicenter epidemiological study of cardiovascular disease (CVD) in 6,914 men and women from 4 ethnic groups—white, African-American, Hispanic, and Chinese—who have been followed for almost 10 years to identify predictors of progression of subclinical CVD. The study originally was funded from 1999 to 2008 and subsequently renewed through 2015. It has measured and compared the predictive value of chest computed tomography, cardiac magnetic resonance imaging, carotid ultrasound, arterial compliance, endothelial function, biochemical markers, and genetic and environmental factors for the development of CVD. MESA has major ongoing ancillary studies in the areas of air pollution (funded by the EPA), chronic lung disease, and genetics. MESA SHaRE (SNP Health Association Resource) will combine genome-wide scans with detailed phenotypic information and share these data with the scientific community for genome-wide association analyses.

- For more information, see <http://mesa-nhlbi.org>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*, Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Genomics*
- (E) (NHLBI, NEI)

Culture of Cooperation to Promote Public Health

Research Initiatives to Study Suicidality and Mental Health Needs of U.S. Army Soldiers and Returning Combat Veterans: The high rates of mental health and behavioral adjustment problems among recent U.S. military combat veterans, and the increasing rates of suicide among Army soldiers, are of growing concern. To address these issues, NIH is collaborating with the U.S. Army to evaluate selected groups of soldiers across all phases of Army service, including entry-level training and service, pre-deployment training, deployment and noncombat assignments, post-deployment, and post-separation reintegration to civilian life. The study's intent is to identify modifiable risk and protective factors, as well as moderators, of suicide-related behaviors. NIH also is launching a study of the impact of existing national, state, and local community-based programs addressing the adjustment and mental health needs of recent combat veterans, including returning National Guard, Army Reserve, and newly separated active duty personnel. This initiative will produce new information concerning effective strategies for fostering successful transition from combat to civilian roles for returning service members.

- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-09-140.html>
- For more information, see <http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-09-070.html>
- This example also appears in Chapter 3: *Clinical and Translational Research*
- (E) (NIMH)

Diabetes and Pesticide Exposure/the Agricultural Health Study: Exposure to certain pesticides increased the risk of diabetes in licensed applicators, according to researchers from NIH. The investigation of applicators enrolled in the Agricultural Health Study is the largest study to date to evaluate potential effects of pesticides on diabetes incidence in adults. Because previous studies using

data from the National Health and Nutrition Examination Survey (NHANES) found associations of diabetes with serum levels of persistent organic pollutants, the researchers wanted to know if there was a similar association between diabetes and lifetime exposure to pesticides. Therefore, they evaluated applicators who reported diabetes for the first time in 5-year follow-up telephone interviews, conducted between 1999 and 2003. Previously, applicators had described use of 50 different pesticides, providing information on 2 primary measures: ever use and cumulative lifetime days of use. Of 50 pesticides evaluated, 7 were associated with an increased incidence of diabetes using both exposure measures. Three of these were organochlorine insecticides (aldrin, chlordane, heptachlor), 2 were organophosphate insecticides (trichlorfon, dichlorvos), and 2 were herbicides (alachlor, cyanazine). The strongest association was with trichlorfon: Applicators who had used the chemical on more than 10 days in their lifetime had a 2.5-fold increase in risk. Pesticide applicators who reported exposure to these pesticides showed an increased risk of diabetes independent of age, state of residence, and body mass index. The increasing burden of diabetes in populations worldwide warrants an improved understanding of the possible relation of diabetes risk to long-term, low levels of pesticide exposure.

- Montgomery MP, et al. *Amer J Epidemiol* 2008;167:1235-46. PMID: 18343878.
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems*
- (E/I) (NIEHS, NCI)

EARLI, the Early Autism Risk Longitudinal Investigation: EARLI, the Early Autism Risk Longitudinal Investigation, comprises a network of leading autism researchers from three regions across the country. EARLI is following a cohort of 1,200 mothers of children diagnosed with autism who are pregnant or planning a pregnancy. The EARLI network will study how genetics and environmental factors work together to cause autism by studying families who already are affected by autism. Data will be collected prospectively via clinical assessment, interviews, self-reports, medical record review, home environment assessments, and biologic samples that will be used in current analysis and stored for future studies. Planned analyses include a determination of whether in utero exposure to organic pollutants such as polychlorinated biphenyls (PCBs), brominated diphenyl ethers (BDEs), and persistent organic pollutants (POPs) is associated with autism risk.

- For more information, see <http://earlistudy.org>
- This example also appears in Chapter 2: *Neuroscience and Disorders of the Nervous System* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIEHS)

Addressing Drug Abuse and Comorbidities in Returning Vets and Their

Families: Sustained U.S. combat operations in Afghanistan and Iraq have resulted in military personnel experiencing increased numbers and lengths of deployments and greater exposure to traumatic stressors. Stress can be a major contributor to both the onset and exacerbation of substance abuse and other mental health problems, and can lead to relapse in former substance abusers. To understand better the intervention needs of this group, NIH in 2009 sponsored a 2-day meeting to formulate a research agenda for conducting addiction prevention and treatment research with military and veteran populations and their families. Collaborators included the U.S. Army Medical Research and Materiel Command, the Department of Defense Health Affairs, the Army Center for Substance Abuse Programs, the Department of Veterans Affairs, and several NIH ICs. Subsequently, a call for studies on trauma, stress, and substance use and abuse among U.S. military personnel, veterans, and their families was issued. It focuses on epidemiology/etiology, screening and identification, and prevention and treatment of substance use and abuse—including alcohol, tobacco, and other drugs—and

associated problems (e.g., PTSD, traumatic brain injury, sleep disturbances, and relationship violence) among U.S. military personnel, veterans, and their families. Further, NIH's National Drug Abuse Treatment Clinical Trials Network (CTN) is developing a protocol concept for the treatment of PTSD and drug abuse/dependence in veteran populations. It is expected that this study will be conducted in clinics participating in the CTN, which include some Veterans Administration hospitals and research facilities.

- For more information, see <http://www.drugabuse.gov/pdf/tib/veterans.pdf>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 2: *Life Stages, Human Development, and Rehabilitation*
- (E) (NIDA, NCI, NIAAA, NIMH)

Health Care Delivery Consortia to Facilitate Discovery and Improve Quality of Cancer

Care: The purpose of the Cancer Research Network (CRN) is to enhance research on cancer epidemiology, prevention, early detection, and control in the context of health care delivery systems. CRN combines established research groups affiliated with 14 health care delivery organizations that provide comprehensive care to a racially and ethnically diverse population of nearly 11 million individuals. CRN has developed strong research capabilities in several areas: developing and applying innovative methods to collect and interpret data from both conventional and electronic medical records systems; assembling large samples of patients with documentation of patient characteristics and longitudinal data on receipt of health services and clinical and quality-of-life outcomes; collecting and integrating complex data from patients, providers, and organizations to examine issues in health care delivery from multiple perspectives; quantifying the effect of key factors in the delivery process that may determine quality and outcomes of care; and conducting studies on behavioral and systems-based interventions to improve the delivery of care in community-based health care delivery systems. The Breast Cancer Surveillance Consortium (BCSC) is a research resource for studies designed to assess the delivery and quality of breast cancer screening and related patient outcomes in the United States. The BCSC is a collaborative network of seven mammography registries with linkages to tumor and/or pathology registries. The Consortium's database contains information on 7,521,000 mammographic examinations, 2,017,869 women, and 86,700 cancer cases.

- For more information, see <http://crn.cancer.gov>
- For more information, see <http://breastscreening.cancer.gov/>
- This example also appears in Chapter 2: *Cancer*, Chapter 3: *Clinical and Translational Research* and Chapter 3: *Disease Registries, Databases, and Biomedical Information Systems*
- (I) (NCI)

Population Genomics, GAIN, and GEI: In 2006, HHS announced the creation of two groundbreaking initiatives for population genomics research in which NIH played a leading role. The Genetic Association Information Network (GAIN) was a public-private partnership involving NIH, the Foundation for NIH, Pfizer, Affymetrix, Perlegen, the Broad Institute, and Abbott. GAIN supported a series of genome-wide association studies designed to identify specific points of DNA variation associated with the occurrence of common diseases. Investigators from existing clinical studies were invited to submit samples and data on roughly 2,000 participants for genomic assays designed to capture roughly 80 percent of the common changes in the human genome. GAIN successfully concluded in November 2008, with the third and final public workshop on the project. At this meeting, investigators from across the research community shared their findings and discussed how they had used the data generated through GAIN in their own research. Data from the GAIN studies have been deposited into the NIH database of Genotype and Phenotype (dbGaP) for the broad use of the research community. Access is controlled by the GAIN Data Access Committee. Additionally, NIH funds the Genes,

Environment, and Health Initiative (GEI), an NIH-wide effort combining comprehensive genetic analysis and environmental technology development to understand the causes of common diseases. GEI has held a number of workshops to identify novel ways of analyzing the wealth of information gathered and to use that data to improve human health.

- For more information, see <http://www.genome.gov/19518664>
- For more information, see <http://www.genome.gov/19518663>
- For more information, see <http://genesandenvironment.nih.gov>
- For more information, see <http://www.genome.gov/11511175>
- This example also appears in Chapter 3: *Genomics*
- (E, I) (NHGRI, NIEHS, NLM)

Urology Research: The Urinary Incontinence Treatment Network (UITN) conducts long-term studies and clinical trials of the most commonly used surgical, pharmacological, and behavioral approaches for management of urinary incontinence in women diagnosed with stress and mixed incontinence. Recently, a different group of investigators completed the Program to Reduce Incontinence by Diet and Exercise (PRIDE) study and determined that a weight loss program could reduce significantly the frequency of urinary incontinence in overweight and obese women. Several studies address interstitial cystitis/painful bladder syndrome (IC/PBS), a urologic condition whose prevalence is uncertain and which remains difficult to diagnose and treat. The RAND Interstitial Cystitis Epidemiology (RICE) study is designed to estimate the prevalence of interstitial cystitis and establish a working definition of this condition. The Boston Area Community Health (BACH) Survey is a population-based study of urologic conditions, including IC/PBS, in more than 5,500 adults. Results emerging from BACH about IC/PBS will provide a clearer picture on the IC/PBS burden in the population, and will inform research efforts to reverse this burden. The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network is designed to enhance understanding of the major urological chronic pelvic pain disorders, including IC/PBS and chronic prostatitis/chronic pelvic pain syndrome.

- Burgio KL, et al. *Ann Int Med* 2008;149:161-9. PMID: 18678843.
- Subak LL, et al. *N Eng J Med* 2009;360(5):481-90. PMID: 19179316.
- For more information, see <http://www.uitn.net/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Clinical and Translational Research*
- (E) (NIDDK, NICHD)

According to a Government Survey, 38 Percent of Adults and 12 Percent of Children Use Complementary and Alternative Medicine:

In December 2008, NIH and the National Center for Health Statistics released new findings on Americans' use of complementary and alternative medicine (CAM). The findings are from the 2007 National Health Interview Survey (NHIS), an annual in-person survey of Americans regarding their health- and illness-related experiences. According to the survey, approximately 38 percent of adults and nearly 12 percent of children use some form of CAM. For both adults and children, the most commonly used type of CAM is nonvitamin/nonmineral natural products, and the most common use for CAM is to treat pain. Although overall use of CAM among adults has remained relatively stable since 2002 (the last time NHIS included a CAM section), the use of some specific CAM therapies has varied substantially; for example, deep breathing, meditation, massage therapy, and yoga have all shown significant increases. The 2007 NHIS was the first to ask about CAM use by children. The NHIS also reports on characteristics of CAM users, such as gender, age, education, geographic region, poverty status, and health indicators. The 2007 NHIS provides the most current, comprehensive, and reliable source of information on Americans' use of CAM. These statistics

confirm that CAM practices are a frequently used component of American's health care regimens, and reinforce the need for rigorous research to study the safety and effectiveness of these therapies. The data also point out the need for patients and health care providers to openly discuss CAM use to ensure safe and coordinated care. Future analyses of these data may help explain some of the observed variation in the use of individual CAM therapies and provide greater insights into CAM use patterns among Americans.

- Barnes PM, et al. *Natl Health Stat Report* 2008;(12):1-23. PMID: 19361005.
- For more information, see <http://www.cdc.gov/nchs/data/nhsr/nhsr012.pdf>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Molecular Biology and Basic Research*
- (E) (NCCAM, CDC)

Half of Surveyed Physicians Use Placebo Treatments for Patients: Treating patients with placebos has a long, complicated, and often controversial history. Nonetheless, little actually is known about U.S. physicians' current attitudes toward and use of placebo treatments. A national survey funded in part by NIH looked at placebo-prescribing practices among 679 internists and rheumatologists—specialties that commonly treat patients with debilitating chronic conditions. The survey found that about half of the physician respondents prescribed placebo treatments on a regular basis. Most (62%) said they think the practice is ethical. Among physicians who prescribed placebos, few said they used inert treatments such as saline injections or sugar pills; they were more likely to recommend over-the-counter analgesics (41%) or vitamins (38%), and some used antibiotics (13%) or sedatives (13%) as placebos. The survey also found that the physicians who used placebos rarely described them as such to patients. Instead, physicians most commonly described the treatments as medicine that typically is not used for the patient's condition but that might be beneficial. The survey provides insights into the complex relationship between placebo use and physicians' traditional role in promoting positive expectations in their patients. It also raises concerns about the use of "active" placebos, particularly antibiotics and sedatives, when they are not medically indicated. Prescribing placebo treatments remains an appropriate topic for ethical and policy debates.

- Tilburt JC, et al. *BMJ* 2008 Oct 23;337:a1938. PMID: 18948346. PMCID: PMC2572204.
- For more information, see <http://nccam.nih.gov/research/results/spotlight/102408.htm>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Molecular Biology and Basic Research*
- (E) (NCCAM)

Study Shows One-Fifth of Internet-Available Ayurvedic Medicines Contain Toxic

Metals: Ayurveda, a traditional medical system that originated in India, aims to integrate and balance the body, mind, and spirit to help prevent illness and promote wellness. Potentially toxic metals sometimes are incorporated in traditional Ayurvedic medicines as part of rasa shastra—a practice that combines herbs with metals, minerals, and gems. In an NIH-funded study, researchers sought to determine how often Ayurvedic medicines sold on the Internet contain detectable levels of lead, mercury, and arsenic. They purchased products manufactured in both India and the United States and examined both rasa shastra and nonrasa shastra (herbal-only) medicines. Using 5 different search engines, the researchers found 25 websites that sold traditional Ayurvedic herbs, formulas, and ingredients. Of the 230 products randomly selected for purchase, 193 were received and tested for the presence of metals. Nearly 21 percent of the Ayurvedic medicines tested were found to contain detectable levels of lead, mercury, or arsenic. Rasa shastra products were more than twice as likely as nonrasa shastra products to contain metals, and several rasa shastra medicines manufactured in India could result in lead and/or

mercury ingestion 100 to 10,000 times greater than acceptable limits. This study's findings lend support to the value and importance of rigorous standards of product quality and self-regulation within the herbal medicine and dietary supplement industry. The authors call for strictly enforced, government-mandated, daily-dose limits for toxic metals in all dietary supplements, and requirements that all manufacturers demonstrate compliance through third-party testing.

- Saper RB, et al. *JAMA* 2008;300(8):915-23. PMID: 18728265. PMCID: PMC2755247.
- For more information, see <http://nccam.nih.gov/research/results/spotlight/082808.htm>
- (E) (NCCAM)

SNP-Health Association Resource (SHARe): SHARe conducts genome-wide association studies in several large NIH cohort studies to identify genes underlying cardiovascular and lung diseases and other disorders such as obesity and diabetes. The resulting genotype data along with the cohort phenotype data are made available to researchers around the world through the NIH dbGAP database. Framingham SHARe, with 9,000 participants, was the first cohort released in this initiative due to its uniqueness in including 3 generations of participants with comparable data obtained from each generation at the same age. As of October 31, 2009, 95 projects to use these data had been approved. A modified version of the dataset was distributed to 72 approved research projects as the focus of a Southwest Foundation Genetic Analysis Workshop. The second cohort released was the SHARe Asthma Resource Project, which includes genotype data from more than 2,500 adults and children who have participated in NIH clinical research trials on asthma. As of October 31, 2009, 11 projects to use these data had been approved. Data from more than 12,000 African-American and Hispanic women from the Women's Health Initiative and approximately 8,300 participants from the Multi-Ethnic Study of Atherosclerosis were released in January 2010.

- For more information, see <http://www.nih.gov/news/pr/oct2007/nhlbi-01.htm>
- For more information, see <http://nih.gov/news/health/dec2008/nhlbi-15.htm>
- For more information, see <http://view.ncbi.nlm.nih.gov/dbgap/>
- This example also appears in Chapter 2: *Chronic Diseases and Organ Systems* and Chapter 3: *Genomics*
- (E) (NHLBI, NLM)